FILE 'HOME' ENTERED AT 10:18:00 ON 03 MAY 2004)

FILE 'MEDLINE, CANCERLIT, BIOTECHDS, EMBASE, CAPLUS' ENTERED AT 10:18:25 ON 03 MAY 2004

L1	217588	S	TUMOR SUPPRESSOR GENE OR P53 OR RB
L2	47380	S	RETROVIR? AND (IN VITRO OR EX VIVO OR CULTURED OR CELL LIN?)
L3	1406	S	L1 AND L2
L4	5155116	S	LEUKEUMIA OR BLOOD OR BONE MARROW OR HEMATOPOIETIC
L5	150	S	L4 AND L3
L6	3404355	S	TUMOR OR CANCER OR METAST?
L7	110	S	L6 AND L5
L8	1213838	S	PURG? OR IMPLAN? OR TRANSPLA?
L9	38	S	L8 AND L7
L10	20		DUP REM L9 (18 DUPLICATES REMOVED)

L10 ANSWER 19 OF 20 MEDLINE on STN DUPLICATE 8
AN 92083531 MEDLINE
DN PubMed ID: 1727382
TI Suppression of acute lymphoblastic leukemia by the human wild-type **p53** gene.
AU Cheng J; Yee J K; Yeargin J; Friedmann T; Haas M
CS UCSD Cancer Center, Department of Pathology, La Jolla 92093-0063.
SO Cancer research, (1992 Jan 1) 52 (1) 222-6.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199201
ED Entered STN: 19920209
Last Updated on STN: 19970203
Entered Medline: 19920117
AB Independent mutations in both alleles of the **p53 tumor suppressor gene** are a frequent finding in human T-cell acute lymphoblastic leukemia (T-ALL) **cell lines** and in the cells of some T-ALL patients in relapse. One major goal of studying the status of **p53** (and other **tumor** suppressor genes) in human **cancer** is to facilitate the suppression of the tumorigenic phenotype through the restoration of the expression of the wild-type allele. While the efficient insertion of a suppressor into all cells of solid/**metastatic** human tumors may at present be impossible, insertion into leukemia cells may be feasible due to the accessibility of the leukemia cells in the body. To examine the feasibility of suppressing the tumorigenicity of human T-leukemia cells, the human T-ALL **cell line** Be-13, which lacks endogenous **p53** protein, was infected with a recombinant **retrovirus** encoding the wild-type allele of human **p53** (hwtp53). Expression of **p53** reduced the growth rate of infected Be-13 cells in **vitro**, suppressed colony formation in methylcellulose cultures, and abrogated their tumorigenic phenotype in nude mice in vivo. These results suggest that suppression of the leukemic phenotype of relapse T-ALL-derived Be-13 cells is feasible. Acute leukemia cell suppression via high-efficiency infection with **retroviruses** encoding wtp53 may be feasible and beneficial in T-ALL cases as part of a **bone marrow transplantation** regimen in an effort to reduce the frequency of posttransplantation relapse.

L10 ANSWER 16 OF 20 MEDLINE on STN DUPLICATE 5
AN 1998133164 MEDLINE
DN PubMed ID: 9472561
TI Expression of exogenous wt-**p53** does not affect normal hematopoiesis: implications for **bone marrow purging**.
AU Scardigli R; Bossi G; Blandino G; Crescenzi M; Soddu S; Sacchi A
CS Molecular Oncogenesis Laboratory, Regina Elena Cancer Institute, Rome, Italy.
SO Gene therapy, (1997 Dec) 4 (12) 1371-8.
Journal code: 9421525. ISSN: 0969-7128.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
ED Entered STN: 19980312
Last Updated on STN: 19980312
Entered Medline: 19980303
AB Some gene therapy approaches for **cancer** treatment attempt to transduce onco-suppressor genes into **tumor** cells. A central problem of this strategy is the targeting of **tumor** cells to avoid damage to normal ones. It has been noticed that transduction of wt-**p53** into a large number of **cancer** cells induces **tumor** suppression. In contrast, some observations suggest that introduction of exogenous wt-**p53** into nontransformed cells does not impair proliferation. If normal **bone marrow** (BM) cells are not affected by wt-**p53** transduction, BM **purging** from **p53**-responding leukemic cells might be achieved in **vitro** by delivering the wild-type onco-suppressor to all marrow cells. We undertook a series of experiments to assess whether transduction of wt-**p53** into normal **hematopoietic** cells is harmful. Two different wt-**p53**-recombinant **retroviruses** were used to infect primary, murine BM cells. Expression of exogenous wt-**p53** in these cells did not affect in **vitro** colony formation, and did not induce any observable effects on morphology and differentiation. In contrast, the same viruses suppressed the **tumor** phenotype of v-src-transformed 32D cells. These results might open the way to gene therapy approaches to leukemias with the **p53** gene without the need to target specifically and uniquely the **tumor** cells, sparing the normal ones.

d bib ab 1-20

L10 ANSWER 1 OF 20 MEDLINE on STN
AN 2004025526 MEDLINE
DN PubMed ID: 14724570
TI Wild-type **p53** gene transfer is not detrimental to normal cells in vivo: implications for **tumor** gene therapy.
AU Bossi Gianluca; Mazzaro Giuseppina; Porrello Alessandro; Crescenzi Marco; Soddu Silvia; Sacchi Ada
CS Department of Experimental Oncology, Molecular Oncogenesis Laboratory, Regina Elena Cancer Institute, Via delle Messi d'Oro 156, Rome 00158, Italy.
SO Oncogene, (2004 Jan 15) 23 (2) 418-25.
Journal code: 8711562. ISSN: 0950-9232.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200402
ED Entered STN: 20040116
Last Updated on STN: 20040204
Entered Medline: 20040203
AB The **p53** oncosuppressor is strictly maintained in an inactive form under normal conditions, while it is post-translationally activated by a variety of stresses, enacting different protective biological functions. Since one critical issue in **cancer** gene therapy is **tumor** specificity, we asked whether the tight **p53** regulation applies also to exogenously transferred **p53**. In principle, this type of regulation could allow **p53** gene transfer in both normal and **tumor** cells to produce detrimental effects only in the latter ones. Here, we report that primary **bone marrow** cells infected with a **p53** recombinant **retrovirus** and **transplanted** into irradiated mice reconstitute the **hematopoietic** system, with no detectable alterations in any of its compartments. Furthermore, simultaneous infection of leukemia and **bone marrow** cells depleted the neoplastic contamination, allowing lifelong, disease-free survival of 65% of the **transplanted** animals. These results show that exogenous **p53** is controlled as tightly as the endogenous one, and opens the way to **p53** gene therapy, without requiring **tumor** targeting.